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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 13-OCT-1999

SUBJECT: PP# 7E4861. Myclobutanil in/on Beans. **Amendment of 4/24/98. Evaluation of Confined Rotational Crop Study**. MRID# 44621901. Chemical 128857. Barcode D250160. Case 289009. Submission# S549900.

FROM: Jennifer E. Rowell, Chemist Jennifer E. Rowell
Registration Action Branch 1
Health Effects Division (7509C)

THROUGH: George F. Kramer, Ph.D., Chemist
Melba Morrow, D.V.M., Branch Senior Scientist MM 10/15/99
Registration Action Branch 1
Health Effects Division (7509C)

TO: Robert Forrest/Sidney Jackson, PM Team 05
Registration Division (7505C)

IR-4 has submitted an application for a tolerance for residues of the fungicide myclobutanil [α-butyl-α-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile] in/on the snap beans. The proposed tolerance, expressed as the parent compound and its alcohol metabolite (α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile) is:

Snap beans	1.0 ppm

REGULATORY BACKGROUND

The following terms, as defined below, are used interchangeably throughout this review:
(i) **myclobutanil**: RH-3866; α-butyl-α-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile; and
(ii) **alcohol metabolite**: RH-9090; α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile.

Permanent tolerances are currently established for the combined residues of myclobutanil and its RH-9090 metabolite (free and bound) in/on a variety of raw agricultural commodities (RACs) at levels ranging from 0.02 to 25.0 ppm and in meat, milk, poultry, and eggs at levels ranging from

0.02 to 1.0 ppm [40 CFR §180.443(a)].

Time-limited tolerances in conjunction with Section 18 registrations have been established for: artichokes (1.0 ppm; expires 7/31/00); asparagus (0.02 ppm, expires 7/31/00); caneberries (1.0 ppm; expires 12/31/99); cucurbit vegetable group (0.3 ppm, expires 5/30/00); hops, dried (5.0 ppm; expires 12/31/99); peppermint (2.5 ppm, expires 1/31/00); peppers, bell and non-bell (1.0 ppm, expires 7/31/00); spearmint (2.5 ppm, expires 1/31/00); strawberries (0.5 ppm; expires 3/31/00); tomatoes (0.3 ppm, expired 7/28/98); tomato paste (1.2 ppm, expired 7/28/98); and tomato puree (0.6 ppm, expired 7/28/98) [40 CFR §180.443(b)].

Executive Summary of Chemistry Deficiencies

- Additional crop field trials.
- Revised Label.

RECOMMENDATIONS

Provided the label is revised as specified in Conclusions 1 and 3, the residue chemistry database supports the establishment of the following proposed tolerance for the combined residues of the myclobutanil and its metabolite RH-9090 (free and bound):

Beans, snap, succulent	1.0 ppm

However, the registration on snap beans should be conditional until the petitioner submits additional crop field trial data as detailed in Conclusion 2a. A human-health risk assessment will be prepared in a separate document.

CONCLUSIONS

OPPTS GLN 860.1200: Proposed Uses

1. Labels have been provided for use of myclobutanil formulated as Rally® 40W Agricultural Fungicide (EPA Reg No. 707-215) and Nova® 40W Agricultural Fungicide (EPA Reg No. 707-221). **The petitioner should submit a revised label with the appropriate rotational crop restrictions as detailed in this memo (See conclusion 3).** All other deficiencies in the label have been resolved.

OPPTS GLN 860.1500: Crop Field Trials

2a. The geographic representation of the residue data from the submitted crop field trials (MRID# 443382-01) is not adequate. A total of seven trials reflecting the proposed maximum use pattern were conducted in Regions 1 (1 trial), 2 (2 trials), 3 (1 trial), 5 (2 trials), and 11 (1 trial). The current guidance (OPPTS GLN 860.1500, Tables 1 and 5) recommends that a minimum of 8 trials should be conducted for the establishment of a tolerance for snap beans, preferably in Regions 1 (1 trial), 2 (1 trial), 3 (1 trial), 5 (3

trials), 10 (1 trial), and 11 (1 trial). Therefore, two additional residue trials should be performed, preferably in Region 10 (1 trial) and Region 5 (1 trial). **Thus, the crop field trial data support a conditional registration until the additional data are submitted.**

2b. The available data indicate that the combined residues of myclobutanil and its metabolite RH-9090 did not exceed the proposed tolerance level of 1.0 ppm in/on snap beans harvested 0 days following the last of multiple foliar applications, with 5-11 day retreatment intervals, of the 40% WP formulation at 0.50 lb ai/A/season (1x the maximum proposed seasonal rate). **The following tolerance is appropriate for residues of myclobutanil and its alcohol metabolite in/on snap beans:**

Bean, snap, succulent	**1.0 ppm**

2c. A final decision on the appropriate tolerance level will be withheld pending submission of the requisite residue data.

OPPTS GLN 860.1850 and 860.1900: Confined/Field Accumulation in Rotational Crops

3a. The submitted confined rotational crop study is adequate to satisfy data requirements for OPPTS 860.1850 pending label revisions of myclobutanil end-use product labels to specify appropriate plantback restrictions. These data show that residues of myclobutanil and its alcohol metabolite are <0.01 ppm in lettuce with a 120-day plantback interval (PBI), radishes with a 210-day PBI, wheat with a 120-day PBI, and soybeans with a 210-day PBI. Therefore, the results of this study support the establishment of the following PBIs for myclobutanil as follows:

Crop	PBI (Days)
crops included on a myclobutanil label	any time
leafy vegetables	120
root vegetables	210
small grains	120
all other crops	210

A revised label should be submitted with these plantback intervals included.

3b. Because the combined residues of myclobutanil and its alcohol metabolite (RH-9090) were <0.01 ppm in/on all tested commodities at plantback intervals of 210 and 365 days, limited field trials (OPPTS 860.1900) will not be required and rotational commodity tolerances need not be proposed/established provided the registrant amends myclobutanil labels to specify the appropriate plantback intervals for rotational crops. Currently, myclobutanil labels do not specify any rotational crop restriction. Alternatively, the registrant has the option of conducting limited field trials on representative crop groups for which shorter plantback intervals are desired.

DETAILED CONSIDERATIONS

Deficiency - Conclusion 2 (from Memo, N. Dodd, 4/24/98; Barcode D238454)

2. A revised Section B/label must be submitted because the petitioner needs to: (i) propose a preharvest interval for snap beans; (ii) possibly propose rotational crop restrictions based upon the findings of a required confined rotational crop study; and (iii) remove the restrictions "Do not graze animals on treated green forage or stubble" and "Do not use hay or straw for animal feed or bedding" since there are no significant animal feed items involved with this use on snap beans (according to Table 1 in OPPTS 860.1000) and such restrictions are no longer considered practical except for soybean forage, soybean hay, and peanut hay.

Petitioner's Response: A revised label with (i) a 0-day preharvest interval for snap beans; and (ii) the restrictions "Do not graze animals on treated green forage or stubble" and "Do not use hay or straw for animal feed or bedding" removed.

HED's Conclusion: This deficiency is resolved, provided the petitioner submits a revised label with the appropriate rotational crop restrictions as detailed in this memo. All other information has been provided.

Deficiency - Conclusion 8 (from Memo, N. Dodd, 4/24/98; Barcode D238454)

8. The submitted residue data for snap beans are not adequate. The available data indicate that the combined residues of myclobutanil and its metabolite RH-9090 did not exceed the proposed tolerance level of 1.0 ppm in/on snap beans harvested 0 days following the last of multiple foliar applications, with 5-11 day retreatment intervals, of the 40% WP formulation at 0.50 lb ai/A/season (1x the maximum proposed seasonal rate). The combined residues of myclobutanil and its metabolite RH-9090 in/on snap beans treated according to the proposed maximum use pattern ranged from 0.04 to 0.493 ppm. However, the geographic representation of the residue data is not adequate. A total of seven trials reflecting the proposed maximum use pattern were conducted in Regions 1 (1 trial), 2 (2 trials), 3 (1 trial), 5 (2 trials), and 11 (1 trial). The current guidance (OPPTS GLN 860.1500, Tables 1 and 5) specifies that a minimum of 8 trials should be conducted for the establishment of a tolerance for snap beans, and that these trials should be conducted in Regions 1 (1 trial), 2 (1 trial), 3 (1 trial), 5 (3 trials), 10 (1 trial), and 11 (1 trial). Therefore, two additional residue trials are needed: one in Region 10 and 1 in Region 5.

Petitioner's Response: None.

HED's Conclusion: HED reiterates it's previous conclusion. The geographic representation of the residue data from the submitted crop field trials (MRID# 443382-01) is not adequate. A total of seven trials reflecting the proposed maximum use pattern were conducted in Regions 1 (1 trial), 2 (2 trials), 3 (1 trial), 5 (2 trials), and 11 (1 trial). The current guidance (OPPTS GLN 860.1500, Tables 1 and 5) recommends that a minimum of 8 trials should be conducted for the establishment of a tolerance for snap beans, preferably in Regions 1 (1 trial), 2 (1 trial), 3 (1 trial), 5 (3 trials), 10 (1 trial), and 11 (1 trial). Therefore, two additional residue trials should be performed, preferably in Region 10 (1 trial) and Region 5 (1 trial). **Thus, the crop field trial data support a conditional registration until the additional data are submitted.**

The available data indicate that the combined residues of myclobutanil and its metabolite RH-9090 did not exceed the proposed tolerance level of 1.0 ppm in/on snap beans harvested 0 days following the last of multiple foliar applications, with 5-11 day retreatment intervals, of the 40%

WP formulation at 0.50 lb ai/A/season (1x the maximum proposed seasonal rate). **The following tolerance is appropriate for residues of myclobutanil and its alcohol metabolite in/on snap beans:**

Bean, snap, succulent	**1.0 ppm**

A final decision on the appropriate tolerance level will be withheld pending submission of the requisite residue data.

Deficiency - Conclusion 11 (from Memo, N. Dodd, 4/24/98; Barcode D238454)

11. No confined rotational crop study was submitted with this petition. Because snap beans are annual vegetable crops and may be rotated, a confined rotational crop study is required. Depending on the results of the confined rotational crop study, a field accumulation in rotational crops study and rotational crop restrictions on myclobutanil end-use product labels may be needed.

Petitioner's Response: Submission of the following confined rotational crop study:

MRID# 44621901. R. Robinson, Ph.D., R. Hanauer, Ph.D.. ^{14}C-RH-3866: Confined Rotational Crop Study. XenoBioric Laboratories, Inc. and Centre Analytical Laboratories, Inc.

Attached is a review of this study (Attachment 1). This information was compiled by Dynamac Corporation under supervision of RAB1/HED. This review has undergone secondary review by RAB1 and has been revised to reflect current HED policies.

HED's Conclusion: The submitted confined rotational crop study is adequate to satisfy data requirements for OPPTS 860.1850 pending label revisions of myclobutanil end-use product labels to specify appropriate plantback restrictions. These data show that residues of myclobutanil and its alcohol metabolite are <0.01 ppm in lettuce with a 120-day plantback interval (PBI), radishes with a 210-day PBI, wheat with a 120-day PBI, and soybeans with a 210-day PBI. Therefore, the results of this study support the establishment of the following PBIs for myclobutanil:

Crop	PBI (Days)
crops included on a myclobutanil label	any time
leafy vegetables	120
root vegetables	210
small grains	120
all other crops	210

A revised label should be submitted with these plantback intervals included.

Because the combined residues of myclobutanil and its alcohol metabolite (RH-9090) were

<0.01 ppm in/on all tested commodities at plantback intervals of 210 and 365 days, limited field trials (OPPTS 860.1900) will not be required and rotational commodity tolerances need not be proposed/established provided the registrant amends myclobutanil labels to specify the appropriate plantback intervals for rotational crops. Currently, myclobutanil labels do not specify any rotational crop restriction. Alternatively, the registrant has the option of conducting limited field trials on representative crop groups for which shorter plantback intervals are desired.

cc: PP#7E04861, J. Rowell (RAB1)
RDI: M. Morrow (10/13/99), Chemists (10/7/99), G. Kramer (10/7/99).
J. Rowell:806W:CM#2:(703)305-5564:7509C:RAB1

MYCLOBUTANIL
PC Code 128857
(DP Barcode D250160)

Registrant's Response to Residue Chemistry Data Requirements

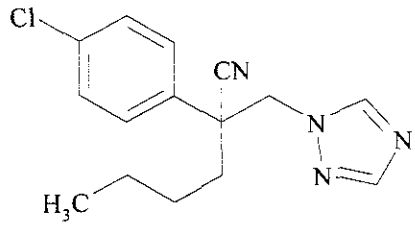
December 7, 1998

Contract No. 68-D4-0010

Submitted to:
U.S. Environmental Protection Agency
Arlington, VA

Submitted by:
Dynamac Corporation
The Dynamac Building
2275 Research Boulevard
Rockville, MD 20850-3268

MYCLOBUTANIL



PC Code 128857

(DP Barcode D250160)

REGISTRANT'S RESPONSE TO RESIDUE CHEMISTRY DATA REQUIREMENTS

BACKGROUND

Rohm and Haas Company has submitted a confined rotational crop study (1998; MRID 44621901) which is evaluated in this document for adequacy in fulfilling the residue chemistry reregistration requirements for OPPTS Guideline No. 860.1850.

The qualitative nature of the residue in plants and animals is adequately understood based on metabolism conducted on wheat, grapes, apples, lactating cows and laying hens. The terminal residues of concern are the parent myclobutanil [α-butyl-α-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile; also referred to as RH-3866] and the free and bound form of RH-9090 metabolite [α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile; also referred to as alcohol metabolite].

Permanent tolerances are currently established for the combined residues of myclobutanil and its RH-9090 metabolite (free and bound) in/on a variety of agricultural commodities at levels ranging from 0.02 to 25.0 ppm and in meat, milk, poultry, and eggs at levels ranging from 0.02 to 1.0 ppm [40 CFR §180.443(a)].

Time-limited tolerances in conjunction with Section 18 registrations have been established for: artichokes (1.0 ppm; expires 7/31/00); asparagus (0.02 ppm, expires 7/31/00); caneberries (1.0 ppm; expires 12/31/99); cucurbit vegetable group (0.3 ppm, expires 5/30/00); hops, dried (5.0 ppm; expires 12/31/99); peppermint (2.5 ppm, expires 1/31/00); peppers, bell and non-bell (1.0 ppm, expires 7/31/00); spearmint (2.5 ppm, expires 1/31/00); strawberries (0.5 ppm; expires 3/31/00); tomatoes (0.3 ppm, expired 7/28/98); tomato paste (1.2 ppm, expired 7/28/98); and tomato puree (0.6 ppm, expired 7/28/98) [40 CFR §180.443(b)].

Rohm and Haas GLC Method 34S-88-10 is available for the purposes of enforcement and data collection. Method 34S-88-10 is a GLC method which determines residues of myclobutanil (using electron capture detection) and the free and bound forms of metabolite RH-9090 (using nitrogen/phosphorus detection) in/on plant matrices. The reported limit of quantitation (LOQ) in plant commodities was 0.02 ppm for each compound. The Agency has conducted successful

validations of Method 34S-88-10, and the method has been forwarded to PAM Vol. II for inclusion as an enforcement method.

CONCLUSIONS AND RECOMMENDATIONS

1. The submitted confined rotational crop study is adequate to satisfy data requirements for OPPTS 860.1850 pending label revisions of myclobutanil end-use product labels to specify appropriate plantback restrictions (see Conclusion No. 6).

2. Except in radish root, sorghum grain, and wheat grain, the total radioactive residues (TRR) accumulated at levels above 0.01 ppm in/on the commodities of radish (top), turnips (top and root), sorghum (forage and straw), wheat (forage and straw), lettuce, mustard (top), and soybeans (forage, straw, and seed) planted 30, 120, 210, and 365 days after treatment (DAT) of sandy loam soil three times with [^{14}C]myclobutanil at 0.2 lb ai/A/application for a total seasonal rate of 0.6 lb ai/A. In general, accumulation of residues decreased with increasing plantback interval. Residues accumulated highest in/on 30-DAT soybean forage (0.151 ppm) and straw (0.232 ppm).

3. All mature raw agricultural commodities (RACs) with TRR levels ≥0.01 ppm were subjected to solvent extraction and fractionation procedures prior to chromatography analysis. In crops planted at a 30-day PBI, the parent myclobutanil was detected in the respective organic fractions of analyzed commodities. Myclobutanil's distribution level ranged from 3.29% TRR in soybean straw to 38.40% TRR in sorghum stover; the magnitude of myclobutanil residues ranged from 0.004 ppm in radish top to 0.027 ppm in soybean forage. RH-9090, the alcohol metabolite, was detected in most crops and its distribution level ranged from 1.57% TRR in soybean seed to 14.79% TRR in sorghum forage; the magnitude of RH-9090 residues ranged from 0.001 ppm in soybean seed to 0.030 ppm in soybean straw. RH-9089, the ketone metabolite, was present in limited amounts and in a few commodities with levels ranging from 1.37% TRR in soybean forage to 11.00% TRR in radish top; the magnitude of RH-9089 residues ranged from 0.002 ppm in soybean forage to 0.006 ppm in radish top. Except for lower magnitude of residues, the nature of residues identified and characterized in/on rotational commodities reflecting other plantback intervals (i.e., 120, 210, and 365 days) were in essence similar to those commodities from the 30-day PBI.

4. The highest levels of residues in 30-DAT commodities were polar residues whose distribution ranged from 18.31% TRR in soybean straw to 51.59% TRR in soybean forage and whose magnitude varied from 0.010 ppm in soybean seed to 0.078 ppm in soybean forage. Following a series of isolation, purification, and chromatographic procedures, the major polar soybean forage metabolites were characterized as the RH-9090 glucoside (Metabolite A) and glucose isomer of Metabolite A (Metabolite B); the major polar soybean straw metabolite was characterized as the carboxylic acid degradate of myclobutanil. Refer to Figure 1 for chemical structures of metabolites identified and characterized.

5. Following initial and solvent extraction/fractionation procedures, the magnitude of nonextractable residues were ≤0.039 ppm except for 30-DAT soybean straw (60.44%

TRR, 0.140 ppm). Attempts to characterize bound residues in 30-DAT soybean forage and straw, using a combination of enzymes (cellulase or protease), acids (1 or 6 N HCl), and base (6 N NaOH), were only moderately successful. RP-HPLC analysis of acid-released residues indicated the presence of predominantly polar residues along with trace levels of myclobutanil.

6. The submitted confined rotational crop study is adequate to satisfy data requirements for OPPTS 860.1850 pending label revisions of myclobutanil end-use product labels to specify appropriate plantback restrictions. These data show that residues of myclobutanil and its alcohol metabolite are <0.01 ppm in lettuce with a 120-day plantback interval (PBI), radishes with a 210-day PBI, wheat with a 120-day PBI, and soybeans with a 210-day PBI. Therefore, the results of this study support the establishment of the following PBIs for myclobutanil:

Crop	PBI (Days)
crops included on a myclobutanil label	any time
leafy vegetables	120
root vegetables	210
small grains	120
all other crops	210

A revised label should be submitted with these rotational crop restrictions included. Because the combined residues of myclobutanil and its alcohol metabolite (RH-9090) were <0.01 ppm in/on all tested commodities at plantback intervals of 210 and 365 days, limited field trials (OPPTS 860.1900) will not be required and rotational commodity tolerances need not be proposed/established provided the registrant amends myclobutanil labels to specify the plantback intervals for rotational crops. Currently, myclobutanil labels do not specify any rotational crop restriction. Alternatively, the registrant has the option of conducting limited field trials on representative crop groups for which shorter plantback intervals are desired.

DETAILED CONSIDERATIONS

Registered Use Patterns

A REFS search, conducted on 11/13/98, identified the following myclobutanil end-use products which are registered under FIFRA Section 3 to Rohm and Haas: 60% DF (EPA Reg. No. 707-211 accepted 2/2/89), 2.25% WP (EPA Reg. No. 707-235 accepted 6/19/97), 40% WP (EPA Reg. Nos. 707-212 accepted 3/27/97, 707-215 accepted 10/14/97, 707-221 accepted 10/14/97, 707-232 accepted 5/4/98, and 707-253 accepted 5/4/98), 2 lb/gal EC (EPA Reg. No.707-222 accepted 4/13/95), and 0.5% D (EPA Reg. No. 707-261 accepted 8/26/97). Except for the 2 lb/gal EC (EPA Reg. No.707-222), the above myclobutanil formulations are registered for use on fruit trees, grapes, and ornamental plants. The 2 lb/gal EC (EPA Reg. No.707-222) is registered for seed treatment on cottonseed at 0.0195-0.0273 lb ai/100 lbs of seed. Seed treatment is recommended for use at the time of planting. The formulation can be tank mixed with other

registered fungicides and can be pumped or poured directly into the cottonseed treater or diluted with water; application through any type of irrigation system is not recommended. The label prohibits the use of treated seed for food, feed, oil production or any other purpose except planting. The grazing of livestock animals grown from treated cottonseed is also prohibited. No rotational crop restrictions appear on the label.

Myclobutanil formulations are additionally registered under FIFRA Section 24c for use on cucurbit vegetables, and copies of these formulations were unavailable for determination of 1x rate. HED previously recommended for the issuance of a Section 18 exemption for use of myclobutanil on strawberries (DP Barcode D203744, 6/9/94, M.J. Nelson). In conjunction with this Section 18 request, the Rally 40W formulation is proposed for a maximum of 6 broadcast postemergence applications on strawberries grown in CA at 0.0625-0.125 lb ai/A using ground equipment. Petitions for the establishment of tolerances for myclobutanil residues of concern in/on snap beans (PP#7E04861, DP Barcode D238454, 4/24/98, N. Dodd) and tomatoes (PP#1F4030/H5616, D203587, 7/13/94, J. Stokes) are currently pending. In conjunction with the snap beans petition, several 40% WP formulations are proposed for multiple foliar applications on snap beans at 0.125 lb ai/A/application; the proposed maximum seasonal rate is 0.5 lb ai/A.

Confined Rotational Crop Study

In-life phase

Rohm and Haas submitted a confined rotational crop study (1998; MRID 44621901). The field phase of the study was conducted outdoors by American Agricultural Services, Inc. (AASI; Lucama, NC) while the analytical phases of the study were conducted by XenoBiotic Laboratories (XBL; Plainsboro, NJ) and Center Analytical Laboratories, Inc. (CAL; State College, PA). Uniformly ring-labeled [^{14}C]myclobutanil (radiochemical purity 99.4%) was mixed with nonlabeled myclobutanil (chemical purity 98.2%) to yield a test substance with a specific activity of 15.07 mCi/g (33,455 dpm/μg). The test substance was applied three times, with a retreatment interval of two weeks, to Norfolk sandy loam soil (42-52% sand, 27-37% silt, 11-29% clay, 0.4-2.0% organic matter, pH 5.0-6.1, cation exchange capacity 7.4-7.5 meq/100 g) as a dilute broadcast spray using a hand-held N_2-pressurized delivery sprayer at a field-equivalent rate of 0.2 lb ai/A/application for a total seasonal rate of 0.6 lb ai/A. Three plots (two treatment and one control) were used in the study. The treatment plots consisted of one large plot (3 x 24 ft; W x L) which was divided into six subplots and one small plot (3 x 4 ft; W x L). The control plot (3 x 28 ft; W x L) consisted of seven subplots (one per crop) and was situated 58 feet from the nearest treatment plot. Representative root crops (radish or turnips), small grains (wheat or sorghum), and leafy vegetables (lettuce or mustard) were planted 30, 120, 210, and 365 days after treatment (DAT). Soybeans were additionally planted at appropriate intervals as a supplemental crop. Rotational crops grew and developed normally without incident with the exception of 30-DAT lettuce which sustained a poor stand and 120-DAT lettuce which suffered a slow die back to ~10% of the total amount seeded. The crops were fertilized and watered as necessary. Adequate information pertaining to the agronomic and climatic conditions during the study was provided. The registrant reported two adverse weather conditions that arose at the field location. Hurricane Bertha arrived at the location on 7/12/96 and Hurricane Fran intersected the area on 9/5/96. Both hurricanes were accompanied by high rainfall (4-5 inches

over a 24- to 48-hour period. The registrant maintains that the test plot integrity was not compromised by either weather event.

Each treated and control crop was sampled at mid-maturity (i.e., immature or intermediate harvest except for 120-DAT lettuce where no intermediate crop sample was taken due to low yield) and at normal crop maturity (i.e., mature or final harvest). The intermediate crop sampling consisted of randomly thinned plants. All remaining plants were harvested at maturity. Intermediate mustard, lettuce, sorghum, soybean, and wheat samples consisted of the entire above ground plant. Radish and turnips were separated into tops and roots. Mature wheat and soybeans were separated into grain and straw, while sorghum was separated into seed and stover. Chaff samples from the wheat and sorghum, and soybean hulls were combined with straw or stover samples, respectively. At AASI, the collected samples were immediately processed (i.e., homogenized to a fine homogenous powder by grinding with dry ice), placed in pre-labeled residue bags or plastic containers, and stored frozen prior to shipment overnight on dry ice or via ACDS freezer truck to XBL. At XBL, samples were stored frozen (-10 C) prior to analysis.

Total radioactive residues (TRR)

Subsamples of the rotational crop commodities were further homogenized with mortar and pestle prior to combustion. Triplicate aliquots were analyzed for TRR by liquid scintillation counting (LSC) following combustion. The LSC limit of detection was 0.01 ppm. The TRR in/on treated rotational crop commodities are presented in Table 1.

Table 1. Total radioactive residues (TRR) in/on rotational crops grown in sandy loam soil treated three times with [^{14}C]myclobutanil at 0.2 lb ai/A/application.

Substrate	TRR (ppm [^{14}C]myclobutanil equivalents)							
	30-DAT [a]		120-DAT		210-DAT		365-DAT	
	Immature	Mature	Immature	Mature	Immature	Mature	Immature	Mature
Root crops								
Radish top	0.103	0.058	0.044	0.058	--	--	0.023	0.036
Radish root	0.087	0.046	<0.010	<0.010	--	--	<0.010	<0.010
Turnip top	-- [b]	--	--	--	0.036	0.012	--	--
Turnip root	--	--	--	--	0.043	0.019	--	--
Cereal grains								
Sorghum forage (stover) [c]	0.098	0.049	--	--	--	--	0.018	0.013
Sorghum grain	NA [d]	0.010	--	--	--	--	NA	<0.010
Wheat forage (straw) [c]	--	--	0.028	0.054	0.060	0.037	--	--
Wheat grain	--	--	NA	<0.010	NA	<0.010	--	--
Leafy vegetables								
Lettuce	0.408	0.094	NS [e]	0.022	--	--	0.021	0.023
Mustard top	--	--	--	--	0.036	0.016	--	--
Legume vegetables								
Soybean forage (straw) [c]	0.151	0.232	--	--	0.029	0.044	0.042	0.026

Substrate	TRR (ppm [^{14}C]myclobutanil equivalents)							
	30-DAT [a]		120-DAT		210-DAT		365-DAT	
	Immature	Mature	Immature	Mature	Immature	Mature	Immature	Mature
Soybean seed	NA	0.046	--	--	NA	0.016	NA	0.013

[a] DAT = Days after treatment.
[b] -- signifies that rotational crops were not planted at this plantback interval.
[c] The substrate listed in parentheses is the mature crop matrix.
[d] NA = Not applicable.
[e] NS = No sample.

Except in radish root, sorghum grain, and wheat grain, Table 1 demonstrates that total radioactive residues, expressed as [^{14}C]myclobutanil equivalents, accumulated at levels above 0.01 ppm in/on the commodities of radish (top), turnips (top and root), sorghum (forage and stover), wheat (forage and straw), lettuce, mustard (top), and soybeans (forage, straw, and seed) planted 30, 120, 210, and 365 days after treatment (DAT) of sandy loam soil three times with [^{14}C]myclobutanil at 0.2 lb ai/A/application for a total seasonal rate of 0.6 lb ai/A. In general, accumulation of residues decreased with increasing plantback interval. Residues accumulated highest in/on 30-DAT soybean forage (0.151 ppm) and straw (0.232 ppm).

Extraction of ^{14}C-residues

All mature RACs with TRR levels ≥0.01 ppm were subjected to solvent extraction. Analysis of immature crops not considered RACs was limited to sample combustion and LSC. **Initially**, radioactive residues in 30-DAT sorghum and soybean forages were extracted with methanol (MeOH). The use of MeOH was, however, discontinued in favor of acetonitrile (CH_3CN). Residues in the MeOH extract of 30-DAT sorghum forage were partitioned using ethyl acetate (EtOAc). This practice was also discontinued in favor of the organic concentrate (i.e., CH_3CN:HCl). A typical crop extraction procedure for most commodities is described below.

Residues in rotational crop commodities were extracted by blending a known quantity of samples with CH_3CN:HCl (95:5, v:v) in a Tekmar Tissuemizer® for ~2-4 minutes. The mixture was filtered and the solids were extracted with a fresh volume of CH_3CN:HCl solution. The mixture was re-filtered and the filtrate was combined with the initial CH_3CN:HCl extract. The combined CH_3CN:HCl extract was partitioned twice with hexane (1:1, v:v), and the hexane fractions were concentrated by rotary evaporation and reserved for chromatography analyses. The remaining solids or nonextractable residues were air dried and homogenized. The distribution of the TRR in the extracts and nonextractable fractions was determined by LSC and combustion/LSC, respectively. In general, residues were extractable from all crops at all plantback intervals. Higher levels of TRR were extracted from high moisture crops (i.e., lettuce, radish tops, turnip tops, or forage crops) than dry crops (i.e., soybean or wheat straw).

Slightly different extraction procedures were employed for the isolation and identification of the major and unknown polar metabolites. For this purpose, the 30-DAT soybean forage and straw samples were selected as "marker matrices". Briefly, residues were sequentially extracted with H_2O overnight followed by CH_3CN in a Tekmar Tissuemizer® for 5 minutes, and the mixture was filtered. The residual solids were re-extracted with CH_3CN. The CH_3CN:H_2O extractable residues were partitioned twice with hexane, and the resulting CH_3CN:H_2O-2 fraction was

concentrated by rotary evaporation and then partitioned three times with EtOAc. The EtOAc fractions were combined and concentrated prior to chromatographic analysis or prior to purification by normal phase TLC in preparation for LC/MS assay.

Hydrolysis of nonextractable residues of 30-DAT soybean straw

Enzyme hydrolysis: The nonextractable residues of 30-DAT soybean straw samples were subjected to enzyme hydrolysis. Two subsamples were suspended in either 0.1 M citrate buffer (pH 5) or 0.2 M phosphate buffer (pH 7.5), and the suspended samples were treated with either cellulase or protease and incubated with the addition of the respective enzyme at ~37 C for 24 hours in a shaker. Following incubation, each sample was removed from the incubator and filtered. The filtrate fractions (designated as hydrolysate or AQ-1) were partitioned twice with EtOAc yielding a combined EtOAc and Hydrolysate (AQ-2) fraction, respectively.

Acid hydrolysis: A subsample of the CH_3CN:HCl-2 extract of 30-DAT soybean straw was subjected to acid hydrolysis (1 N HCl for ~1 hour or 6 N HCl for 24 hours) and partitioned three times with methylene chloride (CH_2Cl_2). The aqueous hydrolysate (HCl-1) fraction following initial solvent partition was re-partitioned (3x) with EtOAc. The CH_2Cl_2 and EtOAc extracts were then combined and concentrated.

Acid/base hydrolysis: Subsamples of nonextractable residues of 30-DAT soybean straw were treated with 1 N HCl, heated to reflux for 1 hour, the mixture was allowed to cool, and then filtered. The hydrolysate was partitioned with CH_2Cl_2 (3x) yielding CH_2Cl_2 and HCl-2 fractions. The HCl-2 fraction was partitioned (2x) with EtOAc resulting in EtOAc and HCl-3 fractions which were combined and reserved for chromatography analysis.

The remaining solids (PES-2) were sequentially hydrolyzed with 6 N HCl for 24 hours at reflux temperature and filtered resulting in PES-3 and HCl-3 fractions. The HCl-3 fraction was partitioned (2x) with EtOAc. The remaining solids (PES-3) were hydrolyzed with 1 N NaOH at reflux for 1 hour. The resulting NaOH fraction was partitioned (2x) with EtOAc, and the resulting EtOAc fraction was concentrated and reserved for chromatography analysis.

The distribution of radioactivity in the extracts of rotational crop commodities is presented in Tables 2a (30-day PBI), 2b (120-day PBI), 2c (210-day PBI), and 2d (365-day PBI).

Metabolite characterization and identification

The extracts of rotational crop commodities were subjected to reversed-phase HPLC analysis to determine the number and nature of metabolites present. HPLC analyses were conducted using a Zorbax Rx C-8 column and a gradient mobile phase of acidic water (0.25 mL H_3PO_4/L water):CH_3CN. Identification was achieved by co-chromatography and/or comparison of retention times with those of standards for myclobutanil, RH-9090, and RH-9089. Nonlabeled reference compounds were detected by UV (225 nm), and radioactivity was detected and quantified by fraction collection/LSC.

In crops planted at a 30-day PBI, the parent myclobutanil was detected in the organic fractions of commodities subjected to RP-HPLC analysis. Myclobutanil's distribution level ranged from 3.29% TRR in soybean straw to 38.40% TRR in sorghum stover; the magnitude of myclobutanil residues ranged from 0.004 ppm in radish top to 0.027 ppm in soybean forage. RH-9090, the alcohol metabolite, was detected in most crops and its distribution level ranged from 1.57% TRR in soybean seed to 14.79% TRR in sorghum forage; the magnitude of RH-9090 residues ranged from 0.001 ppm in soybean seed to 0.030 ppm in soybean straw. RH-9089, the ketone metabolite, was present in limited amounts and in a few commodities with levels ranging from 1.37% TRR in soybean forage to 11.00% TRR in radish top; the magnitude of RH-9089 residues ranged from 0.002 ppm in soybean forage to 0.006 ppm in radish top. The highest levels of residues in 30-DAT commodities were polar residues whose distribution ranged from 18.31% TRR in soybean straw to 51.59% TRR in soybean forage and whose magnitude varied from 0.010 ppm in soybean seed to 0.078 ppm in soybean forage. Except for lower magnitude of residues, the nature of residues identified and characterized in/on rotational commodities reflecting other plantback intervals (i.e., 120, 210, and 365 days) were in essence similar to those commodities from the 30-day PBI.

A series of isolation, purification, and chromatographic procedures was conducted to confirm the identification of myclobutanil and the metabolite RH-9090 in 30-DAT soybean forage and straw. The registrant stated that no further identity confirmation was performed on the ketone metabolite, RH-9089, due to its limited presence in selected crops at very low levels. These same procedures were also utilized to characterize unknown polar metabolites. The initial extracts of soybean forage and straw in straw were subjected to preparative RP-HPLC using a Zorbax Rx C-8 column and a gradient mobile phase of 0.025 M HCO_2H:CH_3CN. The RP-HPLC regions comprising the highest radioactivity (myclobutanil, RH-9090, and two early eluting polar metabolites) were separately collected into respective fractions and concentrated. Each collected fraction was reconstituted in CH_3OH and purified by NP-TLC on silica gel plates developed with $CHCl_3$:EtOAc:CH_3OH:HOAc (90:5:5:0.5, v:v:v:v). The regions were scraped, concentrated, and reinjected to RP-HPLC for further clean-up. The major peaks were recollected and reconstituted in CH_3OH for LC/MS analysis. The identity of myclobutanil and RH-9090 was confirmed based on comparative RP-HPLC retention time and mass spectral data in comparison to known standards. The major polar soybean forage metabolites were characterized as the RH-9090 glucoside (Metabolite A) and glucose isomer of Metabolite A (Metabolite B). The major polar soybean straw metabolite was characterized as the carboxylic acid degradate of myclobutanil.

Attempts to release bound residues from the 30-DAT soybean straw samples using enzymes (cellulase) and acid resulted in solubilization of only modest amount of radioactivity. Sequential acid (1 or 6 N HCl) hydrolysis followed by base (6 N NaOH) hydrolysis was successful. RP-HPLC analysis of acid-released residues indicated the presence of predominantly polar residues along with trace levels of myclobutanil.

Summaries of characterized and identified ^{14}C-residues in/on rotational crop commodities are presented in Tables 3a (30-day PBI), 3b (120-day PBI), 3c (210-day PBI), and 3d (365-day PBI). The chemical names and structures of the identified metabolites are presented in Figure 1.

Table 2a. Distribution of total radioactive residues (TRR) in rotational crops planted 30 days in sandy loam soil which was treated three times with [^{14}C]myclobutanil at 0.2 lb ai/A/application.

Fraction	% TRR	ppm	Characterization/Identification [a]		
30-DAT Lettuce (TRR = 0.094 ppm)					
CH_3CN:HCl-1	58.75	0.055	Partitioned with hexane.		
Hexane	0.00	0.000	Not further analyzed (N/A).		
CH_3CN:HCl-2	58.75	0.055	RP-HPLC resolved:		
			Myclobutanil	13.62% TRR	0.013 ppm
			RH-9090	2.56% TRR	0.002 ppm
			Polar metabolites	42.58% TRR	0.040 ppm
Solids	41.25	0.039	N/A.		
30-DAT Radish Top (TRR = 0.058 ppm)					
CH_3CN:HCl-1	69.58	0.040	Partitioned with hexane.		
Hexane	1.96	0.001	N/A.		
CH_3CN:HCl-2	67.62	0.039	RP-HPLC resolved:		
			Myclobutanil	7.07% TRR	0.004 ppm
			RH-9089	11.00% TRR	0.006 ppm
			Polar metabolites	47.65% TRR	0.027 ppm
			Miscellaneous	1.89% TRR	0.001 ppm
Solids	30.42	0.018	N/A.		
30-DAT Radish Root (TRR = 0.046 ppm)					
CH_3CN:HCl-1	49.44	0.023	Partitioned with hexane.		
Hexane	0.00	0.000	N/A.		
CH_3CN:HCl-2	49.44	0.023	RP-HPLC resolved:		
			Myclobutanil	18.18% TRR	0.008 ppm
			RH-9090	7.85% TRR	0.004 ppm
			Polar metabolites	23.41% TRR	0.011 ppm
Solids	50.56	0.023	N/A.		
30-DAT Sorghum Forage (TRR = 0.098 ppm)					
CH_3CN:HCl-1	63.95	0.063	Partitioned with hexane.		
Hexane	2.46	0.002	N/A.		
CH_3CN:HCl-2	61.49	0.061	Partitioned with EtOAc.		
CH_3CN:EtOAc	54.00	0.054	RP-HPLC resolved:		
			Myclobutanil	8.55% TRR	0.008 ppm
			RH-9089	5.14% TRR	0.005 ppm
			RH-9090	14.79% TRR	0.014 ppm
			Polar metabolites	36.60% TRR	0.036 ppm
Aqueous	7.49	0.007	N/A.		
Solids	36.05	0.035	N/A.		
30-DAT Sorghum Stover (TRR = 0.049 ppm)					
CH_3CN:HCl-1	64.29	0.032	Partitioned with hexane.		
Hexane	0.18	<0.001	N/A.		

(continued; footnotes follow)

Table 2a (*30-day PBI, continued*).

Fraction	% TRR	ppm	Characterization/Identification [a]
CH_3CN:HCl-2	64.11	0.032	RP-HPLC resolved: Myclobutanil 38.40% TRR 0.019 ppm Polar metabolites 25.71% TRR 0.013 ppm
Solids	35.71	0.017	N/A.
30-DAT Sorghum Grain (TRR = 0.010 ppm)			
CH_3CN:HCl-1	41.67	0.004	Partitioned with hexane.
Hexane	0.92	<0.001	N/A.
CH_3CN:HCl-2	40.75	0.004	N/A.
Solids	58.33	0.006	N/A.
30-DAT Soybean Forage (TRR = 0.151 ppm)			
CH_3CN:HCl-1 [b]	80.42	0.121	Partitioned with hexane.
Hexane	4.62	0.007	N/A.
CH_3CN:HCl-2 [b]	75.80	0.114	RP-HPLC resolved: Myclobutanil 17.82% TRR 0.027 ppm RH-9089 1.37% TRR 0.002 ppm RH-9090 4.12% TRR 0.006 ppm Polar metabolites * 51.59% TRR 0.078 ppm Miscellaneous 0.89% TRR 0.001 ppm * Following a series of isolation, purification, and chromatographic procedures, the major polar soybean forage metabolites were characterized as the RH-9090 glucoside (Metabolite A) and the glucose isomer of Metabolite A (Metabolite B).
Solids	19.58	0.030	N/A.
30-DAT Soybean Straw (TRR = 0.232 ppm)			
CH_3CN:HCl-1	39.56	0.092	Partitioned with hexane.
Hexane	1.25	0.003	N/A.
CH_3CN:HCl-2	38.31	0.089	RP-HPLC resolved: Myclobutanil 3.29% TRR 0.008 ppm RH-9089 2.09% TRR 0.005 ppm RH-9090 12.78% TRR 0.030 ppm Polar metabolites * 18.31% TRR 0.042 ppm Miscellaneous 1.84% TRR 0.004 ppm * Following a series of isolation, purification, and chromatographic procedures, the major polar soybean straw metabolite was characterized as the carboxylic acid degradate of myclobutanil.
Solids	60.44	0.140	Hydrolyzed with 1 N HCl.
HCl-1	20.63	0.048	Partitioned with CH_2Cl2.

(continued; footnotes follow)

Fraction	% TRR	ppm	Characterization/Identification [a]
CH_2Cl_2	7.03	0.016	Combined with EtOAc fraction.
HCl-2	13.60	0.032	Partitioned with EtOAc.
EtOAc	7.05	0.017	RP-HPLC analysis of the combined CH_2Cl2 and EtOAc extracts (14.09% TRR, 0.033 ppm) resolved: Myclobutanil 2.28% TRR 0.005 ppm RH-9089 0.63% TRR 0.001 ppm RH-9090 1.61% TRR 0.004 ppm Polar metabolites 10.64% TRR 0.024 ppm Miscellaneous 2.56% TRR 0.006 ppm
HCl-3	6.55	0.015	N/A.
Solids	39.81	0.092	Hydrolyzed with 6 N HCl.
HCl-3	25.72	0.059	Partitioned with EtOAc.
HCl-4	15.98	0.037	N/A.
EtOAc	9.73	0.022	RP-HPLC resolved: Myclobutanil 4.64% TRR 0.011 ppm Polar metabolites 5.12% TRR 0.012 ppm
Solids	14.09	0.033	Hydrolyzed with 1 N NaOH. Majority of the remaining residue (0.022 ppm) was removed with only 0.010 ppm (4.37% TRR) remaining bound to solids. Partitioning with EtOAc resulted in 8.48% TRR (0.020 ppm) rendered organosoluble. No additional work was performed on EtOAc fraction.
30-DAT Soybean Seed (TRR = 0.046 ppm)			
CH_3CN:HCl-1	24.28	0.011	Partitioned with hexane.
Hexane	2.01	0.001	N/A.
CH_3CN:HCl-2	22.27	0.010	RP-HPLC resolved: RH-9090 1.57% TRR 0.001 ppm Polar metabolites 20.70% TRR 0.010 ppm
Solids	75.72	0.035	N/A.

a The identification of myclobutanil and RH-9090 in 30-DAT soybean forage and straw was confirmed by LC/MS.
b Soybean forage was extracted using MeOH in place of CH_3CN. Fractions were identified as CH_3CN:HCl-1 and CH_3CN:HCl-2.

Table 2b. Distribution of total radioactive residues (TRR) in rotational crops planted 120 days in sandy loam soil which was treated three times with [^{14}C]myclobutanil at 0.2 lb ai/A/application.

Fraction	% TRR	ppm	Characterization/Identification		
120-DAT Lettuce (TRR = 0.022 ppm)					
CH_3CN:HCl-1	79.68	0.018	Partitioned with hexane.		
Hexane	2.31	0.001	Not further analyzed (N/A).		
CH_3CN:HCl-2	77.37	0.017	RP-HPLC resolved:		
			Myclobutanil	42.57% TRR	0.009 ppm
			RH-9090	2.72% TRR	0.001 ppm
			Polar metabolites	26.76% TRR	0.006 ppm
			Miscellaneous	5.34% TRR	0.001 ppm
Solids	20.32	0.004	N/A.		
120-DAT Radish Top (TRR = 0.058 ppm)					
CH_3CN:HCl-1	75.13	0.044	Partitioned with hexane.		
Hexane	1.62	0.001	N/A.		
CH_3CN:HCl-2	73.51	0.043	RP-HPLC resolved:		
			Myclobutanil	24.72% TRR	0.014 ppm
			Polar metabolites	40.83% TRR	0.024 ppm
			Miscellaneous	7.96% TRR	0.005 ppm
Solids	24.87	0.014	N/A.		
120-DAT Wheat Forage (TRR = 0.028 ppm)					
CH_3CN:HCl-1	78.13	0.022	Partitioned with hexane.		
Hexane	4.03	0.001	N/A.		
CH_3CN:HCl-2	74.10	0.021	RP-HPLC resolved:		
			Myclobutanil	1.92% TRR	0.001 ppm
			Polar metabolites	72.18% TRR	0.020 ppm
Solids	21.87	0.006	N/A.		
120-DAT Wheat Straw (TRR = 0.054 ppm)					
CH_3CN:HCl-1	41.14	0.022	Partitioned with hexane.		
Hexane	0.00	0.000	N/A.		
CH_3CN:HCl-2	41.14	0.022	RP-HPLC resolved:		
			Myclobutanil	2.05% TRR	0.001 ppm
			RH-9090	13.93% TRR	0.008 ppm
			Polar metabolites	21.49% TRR	0.012 ppm
			Miscellaneous	3.67% TRR	0.002 ppm
Solids	58.86	0.032	N/A.		

Table 2c. Distribution of total radioactive residues (TRR) in rotational crops planted 210 days in sandy loam soil which was treated three times with [^{14}C]myclobutanil at 0.2 lb ai/A/application.

Fraction	% TRR	ppm	Characterization/Identification		
210-DAT Mustard Top (TRR = 0.016 ppm)					
CH_3CN:HCl-1	79.98	0.013	Partitioned with hexane.		
Hexane	0.00	0.000	Not further analyzed (N/A).		
CH_3CN:HCl-2	79.98	0.013	RP-HPLC resolved:		
			RH-9089	6.06% TRR	0.001 ppm
			RH-9090	14.67% TRR	0.002 ppm
			Polar metabolites	48.70% TRR	0.008 ppm
			Miscellaneous	10.56% TRR	0.002 ppm
Solids	20.02	0.003	N/A.		
210-DAT Turnip Top (TRR = 0.012 ppm)					
CH_3CN:HCl-1	37.32	0.004	Partitioned with hexane.		
Hexane	0.00	0.000	N/A.		
CH_3CN:HCl-2	37.32	0.004	N/A.		
Solids	62.68	0.008	N/A.		
210-DAT Turnip Root (TRR = 0.019 ppm)					
CH_3CN:HCl-1	61.73	0.012	Partitioned with hexane.		
Hexane	2.35	<0.001	N/A.		
CH_3CN:HCl-2	59.38	0.012	RP-HPLC resolved:		
			Myclobutanil	21.34% TRR	0.004 ppm
			Polar metabolites	14.23% TRR	0.003 ppm
			Miscellaneous	23.82% TRR	0.005 ppm
Solids	38.27	0.007	N/A.		
210-DAT Wheat Forage (TRR = 0.060 ppm)					
CH_3CN:HCl-1	72.04	0.043	Partitioned with hexane.		
Hexane	2.28	0.001	N/A.		
CH_3CN:HCl-2	69.76	0.042	RP-HPLC resolved:		
			Myclobutanil	3.76% TRR	0.002 ppm
			Polar metabolites	65.05% TRR	0.039 ppm
			Miscellaneous	0.95% TRR	0.001 ppm
Solids	27.96	0.017	N/A.		
210-DAT Wheat Straw (TRR = 0.037 ppm)					
CH_3CN:HCl-1	45.06	0.017	Partitioned with hexane.		
Hexane	0.00	0.000	N/A.		
CH_3CN:HCl-2	45.06	0.017	RP-HPLC resolved:		
			Myclobutanil	6.42% TRR	0.002 ppm
			RH-9090	14.29% TRR	0.005 ppm
			Polar metabolites	21.20% TRR	0.008 ppm
			Miscellaneous	3.15% TRR	0.001 ppm

(continued; footnotes follow)

Fraction	% TRR	ppm	Characterization/Identification
Solids	54.94	0.020	N/A.
210-DAT Soybean Forage (TRR = 0.029 ppm)			
CH_3CN:HCl-1	70.35	0.020	Partitioned with hexane.
Hexane	2.15	0.001	N/A.
CH_3CN:HCl-2	68.20	0.019	RP-HPLC resolved: Polar metabolites 68.20% TRR 0.019 ppm
Solids	29.65	0.009	N/A.
210-DAT Soybean Straw (TRR = 0.044 ppm)			
CH_3CN:HCl-1	44.01	0.019	Partitioned with hexane.
Hexane	4.96	0.002	N/A.
CH_3CN:HCl-2	39.05	0.017	RP-HPLC resolved: Myclobutanil 1.50% TRR 0.001 ppm RH-9089 3.07% TRR 0.001 ppm RH-9090 8.95% TRR 0.004 ppm Polar metabolites 25.53% TRR 0.011 ppm
Solids	55.99	0.025	N/A
210-DAT Soybean Seed (TRR = 0.016 ppm)			
CH_3CN:HCl-1	50.99	0.008	Partitioned with hexane.
Hexane	0.50	<0.001	N/A.
CH_3CN:HCl-2	50.49	0.008	N/A.
Solids	49.01	0.008	N/A.

Table 2d. Distribution of total radioactive residues (TRR) in rotational crops planted 365 days in sandy loam soil which was treated three times with [^{14}C]myclobutanil at 0.2 lb ai/A/application.

Fraction	% TRR	ppm	Characterization/Identification
365-DAT Lettuce (TRR = 0.023 ppm)			
CH_3CN:HCl-1	54.47	0.013	Partitioned with hexane.
Hexane	0.00	0.000	Not further analyzed (N/A).
CH_3CN:HCl-2	54.47	0.013	RP-HPLC resolved: Myclobutanil 10.83% TRR 0.003 ppm RH-9089 6.87% TRR 0.002 ppm Polar metabolites 32.80% TRR 0.008 ppm Miscellaneous 3.96% TRR 0.001 ppm
Solids	45.53	0.010	N/A.
365-DAT Radish Top (TRR = 0.036 ppm)			
CH_3CN:HCl-1	74.66	0.027	Partitioned with hexane.
Hexane	0.00	0.000	N/A.

(continued; footnotes follow)

Table 2d (*365-day PBI, continued*).

Fraction	% TRR	ppm	Characterization/Identification		
CH_3CN:HCl-2	74.66	0.027	RP-HPLC resolved:		
			Myclobutanil	10.23% TRR	0.004 ppm
			Polar metabolites	55.62% TRR	0.020 ppm
			Miscellaneous	8.80% TRR	0.003 ppm
Solids	25.34	0.009	N/A.		
365-DAT Sorghum Forage (TRR = 0.018 ppm)					
CH_3CN:HCl-1	71.16	0.013	Partitioned with hexane.		
Hexane	0.00	0.000	N/A.		
CH_3CN:HCl-2	71.16	0.013	RP-HPLC resolved:		
			RH-9089	6.44% TRR	0.001 ppm
			RH-9090	6.25% TRR	0.001 ppm
			Polar metabolites	56.74% TRR	0.011 ppm
			Miscellaneous	1.73% TRR	<0.001 ppm
Solids	28.84	0.005	N/A.		
365-DAT Sorghum Stover (TRR = 0.013 ppm)					
CH_3CN:HCl-1	26.85	0.003	Partitioned with hexane.		
Hexane	4.82	0.001	N/A.		
CH_3CN:HCl-2	22.03	0.002	N/A.		
Solids	73.15	0.010	N/A.		
365-DAT Soybean Forage (TRR = 0.042 ppm)					
CH_3CN:HCl-1	74.55	0.031	Partitioned with hexane.		
Hexane	0.00	0.000	N/A.		
CH_3CN:HCl-2	74.55	0.031	RP-HPLC resolved:		
			Myclobutanil	5.88% TRR	0.002 ppm
			RH-9089	4.29% TRR	0.002 ppm
			Polar metabolites	60.95% TRR	0.026 ppm
			Miscellaneous	3.43% TRR	0.001 ppm
Solids	25.45	0.011	N/A.		
365-DAT Soybean Straw (TRR = 0.026 ppm)					
CH_3CN:HCl-1	43.11	0.011	Partitioned with hexane.		
Hexane	1.55	<0.001	N/A.		
CH_3CN:HCl-2	41.56	0.011	RP-HPLC resolved:		
			RH-9090	3.33% TRR	0.001 ppm
			Polar metabolites	38.22% TRR	0.011 ppm
Solids	56.89	0.015	N/A.		
365-DAT Soybean Seed (TRR = 0.013 ppm)					
CH_3CN:HCl-1	45.72	0.006	Partitioned with hexane.		
Hexane	0.00	0.000	N/A.		
CH_3CN:HCl-2	45.72	0.006	N/A.		

Table 2d (*365-day PBI, continued*).

Fraction	% TRR	ppm	Characterization/Identification
Solids	54.28	0.007	N/A.

Table 3a. Summary of radioactive residues identified and characterized in/on rotational crop commodities planted 30 days following the last of three applications of [^{14}C]myclobutanil at 0.2 lb ai/A/application to sandy loam soil.

Fraction/Metabolite	30-DAT Lettuce (TRR=0.094 ppm)		30-DAT Radish Top (TRR=0.058 ppm)		30-DAT Radish Root (TRR=0.046 ppm)		30-DAT Sorghum Forage (TRR=0.098 ppm)		30-DAT Sorghum Stover (TRR=0.049 ppm)		30-DAT Soybean Forage (TRR=0.151 ppm)	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
Identified												
Myclobutanil [a]	13.62	0.013	7.07	0.004	18.18	0.008	8.55	0.008	38.40	0.019	17.82	0.027
RH-9090 [a]	2.56	0.002	--	--	7.85	0.004	14.79	0.014	--	--	4.12	0.006
RH-9089	--	--	11.00	0.006	--	--	5.14	0.005	--	--	1.37	0.002
Subtotal	***16.18***	***0.015***	***18.07***	***0.010***	***26.03***	***0.012***	***28.48***	***0.027***	***38.40***	***0.019***	***23.31***	***0.035***
Characterized												
Polar metabolites	42.58	0.040	47.65	0.027	23.41	0.011	36.60	0.036	25.71	0.013	51.59 [b]	0.078 [b]
Miscellaneous	--	--	1.89	0.001	--	--	--	--	--	--	0.89	0.001
Subtotal	*42.58*	*0.040*	*49.54*	*0.028*	*23.41*	*0.011*	*36.60*	*0.036*	*25.71*	*0.013*	*52.48*	*0.079*
Total Identified and Characterized	**58.76**	**0.055**	**67.61**	**0.038**	**49.44**	**0.023**	**65.08**	**0.063**	**64.11**	**0.032**	**75.79**	**0.114**
Nonextractable	41.25	0.039	30.42	0.018	50.56	0.023	36.05	0.035	35.71	0.017	19.58	0.030

Fraction/Metabolite	30-DAT Soybean Straw (TRR=0.232 ppm)		30-DAT Soybean Seed (TRR=0.046 ppm)	
	% TRR	ppm	% TRR	ppm
Identified				
Myclobutanil [a]	3.29	0.008	--	--
RH-9090 [a]	12.78	0.030	1.57	0.001
RH-9089	2.09	0.005	--	--
Subtotal	***18.16***	***0.043***	***1.57***	***0.001***
Characterized				
Polar metabolites	18.31[c]	0.042 [c]	20.70	0.010
Miscellaneous	1.84	0.004	--	--
Subtotal	*20.15*	*0.046*	*20.70*	*0.010*
Total Identified and Characterized	**38.31**	**0.089**	**22.27**	**0.011**
Nonextractable	60.44	0.140	75.72	0.035

[a] The identification of myclobutanil and RH-9090 in 30-DAT soybean forage and straw was confirmed by LC/MS.

[b] Following a series of isolation, purification, and chromatographic procedures, the major polar soybean forage metabolites were characterized as the RH-9090 glucoside (Metabolite A) and glucose isomer of Metabolite A (Metabolite B).

[c] Following a series of isolation, purification, and chromatographic procedures, the major polar soybean straw metabolite was characterized as the carboxylic acid degradate of myclobutanil.

Table 3b. Summary of radioactive residues identified and characterized in/on rotational crop commodities planted 120 days following the last of three applications of [^{14}C]myclobutanil at 0.2 lb ai/A/application to sandy loam soil.

Fraction/Metabolite	120-DAT Lettuce (TRR=0.022 ppm)		120-DAT Radish Top (TRR=0.058 ppm)		120-DAT Wheat Forage (TRR=0.028 ppm)		120-DAT Wheat Straw (TRR=0.054 ppm)	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
Identified								
Myclobutanil	42.57	0.009	24.72	0.014	1.92	0.001	2.05	0.001
RH-9090	2.72	0.001	--	--	--	--	13.93	0.008
RH-9089	--	--	--	--	--	--	--	--
Subtotal	***45.29***	***0.010***	***24.72***	***0.014***	***1.92***	***0.001***	***15.98***	***0.009***
Characterized								
Polar metabolites	26.76	0.006	40.83	0.024	72.18	0.020	21.49	0.012
Miscellaneous	5.34	0.001	7.96	0.005	--	--	3.67	0.002
Subtotal	*32.1*	*0.007*	*48.79*	*0.029*	*72.18*	*0.020*	*25.16*	*0.014*
Total Identified and Characterized	**77.39**	**0.017**	**73.51**	**0.043**	**74.1**	**0.021**	**41.14**	**0.023**
Nonextractable	20.32	0.004	24.87	0.014	21.87	0.006	58.86	0.032

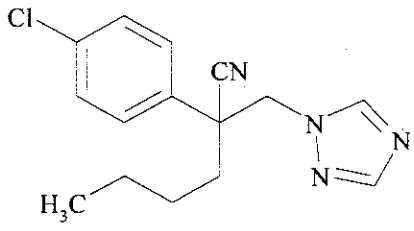
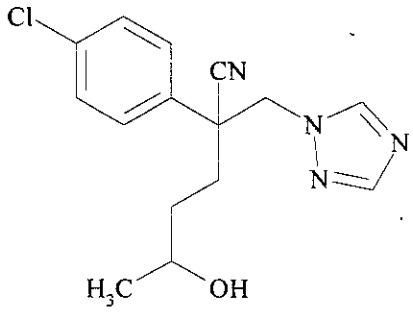
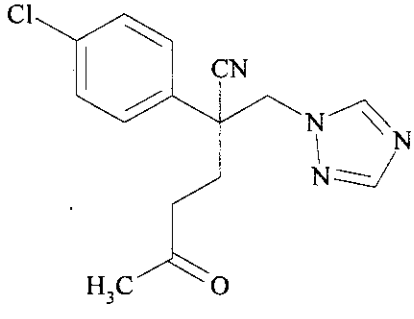
Table 3c. Summary of radioactive residues identified and characterized in/on rotational crop commodities planted 210 days following the last of three applications of [^{14}C]myclobutanil at 0.2 lb ai/A/application to sandy loam soil.

Fraction/Metabolite	210-DAT Mustard Top (TRR=0.016 ppm)		210-DAT Turnip Root (TRR=0.019 ppm)		210-DAT Wheat Forage (TRR=0.060 ppm)		210-DAT Wheat Straw (TRR=0.037 ppm)		210-DAT Soybean Forage (TRR=0.029 ppm)		210-DAT Soybean Straw (TRR=0.044 ppm)	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
Identified												
Myclobutanil	--	--	21.34	0.004	3.76	0.002	6.42	0.002	--	--	1.50	0.001
RH-9090	14.67	0.002	--	--	--	--	14.29	0.005	--	--	8.95	0.004
RH-9089	6.06	0.001	--	--	--	--	--	--	--	--	3.07	0.001
Subtotal	***20.73***	***0.003***	***21.34***	***0.004***	***3.76***	***0.002***	***20.71***	***0.007***	**--**	**--**	***13.52***	***0.006***
Characterized												
Polar metabolites	48.70	0.008	14.23	0.003	65.05	0.039	21.20	0.008	68.20	0.019	25.53	0.011
Miscellaneous	10.56	0.002	23.82	0.005	0.95	0.001	3.15	0.001	--	--	--	--
Subtotal	*59.26*	*0.010*	*38.05*	*0.008*	*66.00*	*0.040*	*24.35*	*0.009*	*68.20*	*0.019*	*25.53*	*0.011*
Total Identified and Characterized	**79.99**	**0.013**	**59.39**	**0.012**	**69.76**	**0.042**	**45.06**	**0.016**	**68.20**	**0.019**	**39.05**	**0.017**
Nonextractable	20.02	0.003	38.27	0.007	27.96	0.017	54.94	0.020	29.65	0.009	55.99	0.025

Table 3d. Summary of radioactive residues identified and characterized in/on rotational crop commodities planted 365 days following the last of three applications of [^{14}C]myclobutanil at 0.2 lb ai/A/application to sandy loam soil.

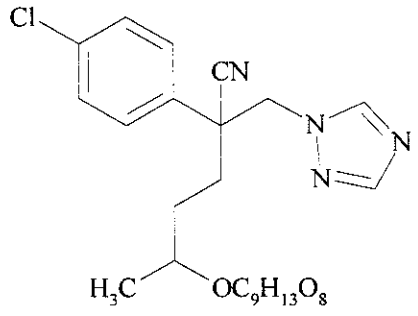
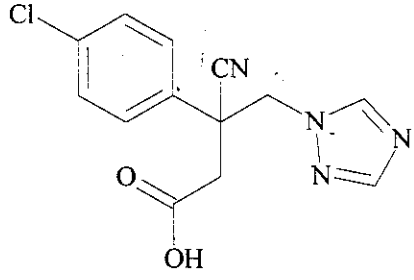
Fraction/Metabolite	365-DAT Lettuce (TRR=0.023 ppm)		365-DAT Radish Top (TRR=0.036 ppm)		365-DAT Sorghum Forage (TRR=0.018 ppm)		365-DAT Soybean Forage (TRR=0.042 ppm)		365-DAT Soybean Straw (TRR=0.026 ppm)	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
Identified										
Myclobutanil	10.83	0.003	10.23	0.004	--	--	5.88	0.002	--	--
RH-9090	--	--	--	--	6.25	0.001	--	--	3.33	0.001
RH-9089	6.87	0.002	--	--	6.44	0.001	4.29	0.002	--	--
Subtotal	***17.70***	***0.005***	***10.23***	***0.004***	***12.69***	***0.002***	***10.17***	***0.004***	***3.33***	***0.001***
Characterized										
Polar metabolites	32.80	0.008	55.62	0.020	56.74	0.011	60.95	0.026	38.22	0.011
Miscellaneous	3.96	0.001	8.80	0.003	1.73	<0.001	3.43	0.001	--	--
Subtotal	*36.76*	*0.009*	*64.42*	*0.023*	*58.47*	*<0.012*	*64.38*	*0.027*	*38.22*	*0.011*
Total Identified and Characterized	**54.46**	**0.014**	**74.65**	**0.027**	**71.16**	**<0.014**	**74.55**	**0.031**	**41.55**	**0.012**
Nonextractable	45.53	0.010	25.34	0.009	28.84	0.005	25.45	0.011	56.89	0.015

Figure 1. Myclobutanil and its metabolites in/on rotational crops.

Common Name Chemical Name	Structure	Substrate
Identified by RP-HPLC		
Myclobutanil; RH-3866 α-butyl-α-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile		Lettuce (30-, 120-, and 365-DAT); Radish Top (30-, 120-, and 365-DAT); Radish root (30-DAT); Sorghum forage (30-DAT); Sorghum stover (30-DAT); Soybean forage (30- and 365-DAT); Soybean straw (30- and 210-DAT); Wheat forage (120- and 210-DAT); Wheat straw (120- and 210-DAT); Turnip root (210-DAT)
RH-9090; alcohol metabolite α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile		Lettuce (30- and 120-DAT); Radish root (30-DAT); Sorghum forage (30- and 365-DAT); Soybean forage (30-DAT); Wheat straw (120- and 210-DAT); Mustard top (210-DAT); Soybean straw (30-, 210- and 365-DAT)
RH-9089; ketone metabolite		Radish top (30-DAT); Sorghum forage (30- and 365-DAT); Soybean forage (30- and 365-DAT); Mustard top (210-DAT); Soybean straw (30- and 210-DAT); Lettuce (365-DAT)

(*continued next page*)

Figure 1 (*continued*).

Common Name Chemical Name	Structure	Substrate
Characterized by LC/MS		
RH-9090 glucoside (Metabolite A)		Soybean forage (30-DAT)
Carboxylic acid degradate of myclobutanil		Soybean straw (30-DAT)

Storage stability

All rotational crop samples were frozen after collection and stored frozen prior to analysis. Crop extracts were stored at a refrigerated temperature (~0-5 C) prior to chromatographic analysis. The storage interval, from crop harvest to initial HPLC analysis, was 20-56 days. To validate the storage stability of samples, residues in subsamples of 30-DAT soybean straw were extracted as described above, and the extracts were analyzed at the study initiation (12/96) and termination (8/97). The levels of myclobutanil, RH-9090, and polar metabolites did not change over the course of study.

Proposed metabolic pathway

Based on the results of the study, the registrant proposed that myclobutanil can be taken up directly from the soil by the plant and oxidatively metabolized at the Ω-1 carbon of the alkyl side chain to the alcohol metabolite, RH-9090. The alcohol metabolite can be conjugated with endogenous sugars to form glucosides and glycosides which in turn can be transported into the

plant cell walls as bound residues. In addition, the alcohol metabolite can be further oxidized to the corresponding ketone metabolite, RH-9089.

Study summary

The submitted confined rotational crop study is adequate to satisfy data requirements for OPPTS 860.1850 pending label revisions of myclobutanil end-use product labels to specify appropriate plantback restrictions.

These data show that residues of myclobutanil and its alcohol metabolite are <0.01 ppm in lettuce with a 120-day plantback interval (PBI), radishes with a 210-day PBI, wheat with a 120-day PBI, and soybeans with a 210-day PBI. Therefore, the results of this study support the establishment of the following PBIs for myclobutanil:

Crop	PBI (Days)
crops included on a myclobutanil label	any time
leafy vegetables	120
root vegetables	210
small grains	120
all other crops	210

A revised label should be submitted with these rotational crop restrictions included. Because the combined residues of myclobutanil and its alcohol metabolite (RH-9090) were <0.01 ppm in/on all tested commodities at plantback intervals of 210 and 365 days, limited field trials (OPPTS 860.1900) will not be required and rotational commodity tolerances need not be proposed/established provided the registrant amends myclobutanil labels to specify the plantback intervals for rotational crops. Currently, myclobutanil labels do not specify any rotational crop restriction. Alternatively, the registrant has the option of conducting limited field trials on representative crop groups for which shorter plantback intervals are desired.

EPA MEMORANDA CITED IN THIS REVIEW

CBTS No.: 15615
DP Barcode: D215688
Subject: PP#2E4141 - Myclobutanil on Bananas. Amendment dated 3/3/95.
From: N. Dodd
To: C. Welch and C. Grable and D. McCall
Dated: 4/4/96

MRID(s): None

DP Barcode: D238454
Subject: PP#7E4861. Myclobutanil on Snap beans. Review of Analytical Method and Residue Data.
From: N. Dodd
To: H. Jamerson and R. Forrest
Dated: 4/24/98
MRID(s): 44338201

CBTS No.: 13799
DP Barcode: D203587
Subject: PP#1F4030/H5616. Amendment Dated 5/12/94. Myclobutanil In/On Tomatoes and Tomato Processed Fractions
From: J. Stokes
To: S. Robbins
Dated: 7/13/94
MRIDs: 43230401

CBTS No.: 13793
DP Barcode: D203744
Subject: Section 18 Exemption for Use of Myclobutanil on Strawberries.
From: M. J. Nelson
To: S. Stanton
Dated: 6/9/94
MRID(s): None

MASTER RECORD IDENTIFICATION NUMBER

The citation for the MRID document referred to in this review is presented below.

44621901 Robinson, R. And Hanauer, R. (1998) ^{14}C-RH3866: Confined Rotational Crop Study. XBL Report No. RPT00399; XBL Study No. XBL96026; Rohm and Haas technical report No. TR 34-98-122. Unpublished study prepared by American Agricultural Services, Inc. (AASI; Lucama, NC), XenoBiotic Laboratories (XBL; Plainsboro, NJ), and Center Analytical Laboratories, Inc. (CAL; State College, PA). 600 p.